Journal of Equine Veterinary Science 32 (2012) 139-145

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

Effects of Topical Application of Sunflower-Seed Oil on Experimentally Induced Wounds in Horses

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A R T I C L E I N F O

Article history:
Received 20 February 2011
Received in revised form
13 May 2011
Accepted 1 August 2011
Available online 15 September 2011

Keywords:
Horses
Sunflower-seed Oil
Wounds
Healing
Phytotherapy

A B S T R A C T

The objectives were to evaluate clinical and histopathological aspects of topical application of sunflower-seed oil (*Helianthus annuus*) on the healing process of experimentally induced wounds in lumbar and metacarpal areas of healthy horses. Six adult horses were used. Eight wounds were surgically produced on each horse: two 6.25-cm^2 wounds cranial to the sacrum on each side of the lumbar region and two 2.89-cm^2 wounds close to the proximal epiphysis of the metacarpus on the lateral aspect of each forelimb. Left side was used for macroscopic observations and right side for histopathological analysis. The experimental lesions were treated daily with sunflower-seed oil, whereas saline solution was used in control lesions. Macroscopic and histopathological analyses were performed on tissue harvested at 3, 7, 14, and 21 days. Complete healing time for all wounds was recorded. For lumbar region's wounds, a contraction of 90.78% was recorded for those treated with oil and of 79.27% for control wounds after 21 days of treatment. For metacarpal region's wounds, a contraction of 47.63% was recorded for wounds treated with oil and of 30.21% for control wounds. Wounds in the sunflower-seed oil treatment group had an elevation of polymorphonuclear cells, a newly formed vascular bed during the inflammatory phase, and a better alignment of collagen fibers during the remodeling phase. In conclusion, topical application of sunflower-seed oil was beneficial in the healing process of experimentally induced skin wounds in horses, with best results for treatment of lumbar wounds, making it a therapeutic option in equine wound healing.

1. Introduction

Araujo et al. [1] and Garros et al. [2] defined a wound as any anatomic alteration of skin integrity as a result of any type of trauma, either intentional (surgical incision) or accidental. Regardless of the etiology, wounds lead to a decrease in blood flow and sensation, the accumulation of inflammatory debris, and variable degrees of contamination (with or without infection) [3].

The dynamic process of healing holds a complex and coordinated sequence of cytological events that interact in repairing and restructuring the tissue, reestablishing the integrity of the skin [4,5]. The healing process starts immediately after the injury and comprises inflammatory, proliferative, and remodeling phases [6-8]. Depending on the type of wound, location, contamination, and tissue viability, the healing can occur by primary or secondary intention or by delayed primary closure [9].

In equine veterinary practice, skin wounds are common [10]. The most commonly affected areas are distal limbs

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doi:10.1016/j.jevs.2011.08.006

(up to and including the carpus and tarsus) and the pectoral region [8]. Horses appear to develop exuberant tissue more frequently compared with other species [11], possibly because of a retarded initial inflammatory response and leukocyte influx [8]. Histological examination has shown that fibroblast proliferation continues even after the wound has been completely filled with granulation tissue [8].

Environmental and physiologic factors have been shown to impact wound healing. Different substances have been used to manage the wound-healing process, including medicinal herbs (phytotherapy), which can be used as primary or secondary therapy. Many studies have been performed in an attempt to show the benefits of using herbs for wound healing in humans and animals [12-14], including using copaiba oil [15], papain [16], sugar [17], barbatimao [18], and passion fruit [2]. Aloe vera, comfrey, eucalyptus, jojoba, and propolis have also been evaluated [19].

Several topical phytotherapic preparations have been used in horses, with some being ineffective or even harmful to the healing process, causing irritation and stimulating the development of exuberant granulation tissue [20]. Experimental reports in equine wound healing using phytotherapy include the use of *Triticum vulgare* cream [21] and barbatimao, calendula, and comfrey [22].

The sunflower (*H annuus*) has been cultivated as an ornamental and medicinal plant in Europe since the 18th century. Research describing the use of sunflowers in wound treatment began in 1929 [23-25]. In human medicine, the topical application has been described for the treatment of burns [26] and pressure sores [27]. Sunflower seeds have oleic acid and abundant unsaturated fatty acids, most prominently linoleic acid, which is a precursor of arachidonic acid [28]. Arachidonic acid is a prominent polyunsaturated fatty acid in the skin, and its functional role depends largely on the generation of biologically potent mediators: prostaglandins, thromboxanes, and leukotrienes. These substances act as inflammatory mediators [5,29], stimulating local neovascularization, cellular migration, and fibroblastic proliferation and differentiation along with extracellular matrix synthesis [30]. Sunflower oil has also been shown to have antibacterial effects [3,29].

Veterinary studies have shown the benefit of sunflower-seed oil in wound healing in both lambs [29] and rats [3]. Wendt [28] compared the effect of sunflower-seed oil and calendula on the healing process of experimentally induced wounds in rabbits and found no differences in the speed of wound contraction. However, there was less exuberant granulation tissue and less fibrosis in wounds treated with the oil. To the authors' knowledge, there has been no research performed in equine wound healing.

The aim of this study was to evaluate the clinical and histopathological aspects of topical application of sunflower-seed oil (*H annuus*) on the healing process of experimentally induced wounds in lumbar and dorsal metacarpal areas of healthy horses. The hypothesis was that sunflower-seed oil would improve the wound-healing process, without stimulation of exuberant granulation tissue.

2. Materials and Methods

The study and procedures were reviewed and approved by the Committee of Ethics of the Centro Universitário Vila Velha, Vila Velha, Espirito Santo, Brazil (64/2009). The study included six adult crossbred horses (three males and three females) weighing between 350 and 420 kg, with ages ranging from 7 to 12 years. All horses were considered normal based on physical examination (no skin abnormalities present), complete blood cell count, serum biochemistry, and parasitological examination. Horses were maintained at Clube do Cavalo of Alfredo Chaves city, Espirito Santo, Brazil, where they were adapted for a 2-week period before the onset of the study. Each animal was dewormed with ivermectin (200 μg/kg body weight orally), and dentistry was performed to remove any sharp points from their teeth. The horses were vaccinated against equine influenza, tetanus, and encephalomyelitis (Tri-Equi-Hertap Hertape Calier Saúde Animal, Juatuba, MG, Brazil).

Horses were fed according to Ralston [31] with coast-cross grass hay (*Cynodon dactylon*) ad libitum and commercial concentrate feed with 12% protein (1% body weight). Water was given ad libitum.

Hay and commercial feed were withheld from all horses for 12 hours before surgery. All horses had free access to water. Horses were sedated with xylazine 10% (1 mg/kg, intravenously) and placed in restraining stocks. Local anesthesia was achieved using lidocaine 2% without epinephrine. In the lumbar area, an inverted U block was performed, and in the metacarpal region, a ring block near the proximal epiphysis of the metacarpus was used.

Both sides of lumbar area and lateral aspects of metacarpal regions were clipped and aseptically prepared using povidone-iodine 5% solution and 70% alcohol. Eight wounds were surgically produced on each horse: two 6.25-cm^2 (2.5 $\times$ 2.5 cm^2) wounds cranial to the sacrum on each side of the lumbar region (ventral to L1-L6: lumbar vertebrae) and two 2.89-cm^2 (1.7 $\times$ 1.7 cm^2) wounds close to the proximal epiphysis of the metacarpus on the lateral aspect of each forelimb. Excision depth included skin and subcutaneous tissue. All wounds were measured using a digital pachymeter (Starrett 727–6/150; L.S. Starrett Company, CA, USA). After surgery, all horses were given phenylbutazone (4.4 mg/kg, intravenously) every 24 hours for 3 days to control edema and pain [32].

Treatment began 12 hours after surgery and was repeated twice daily until total wound healing. Horses were randomly assigned into treatment groups. In three horses, the cranial lumbar wounds on both sides of midline were used for the treatment group, and in the other three horses, the caudal lumbar wounds on both sides of midline were used for the treatment group. In both cases, the other wounds were used as a control. In the treatment group, the wounds were rinsed with physiologic saline solution and covered with gauze containing sunflower-seed oil (experimental wounds sunflower-seed oil Sinhá lote L 0410 GRP 201468, Brazil). In the control group, the wounds were rinsed with physiologic saline solution and covered with gauze containing saline solution (control wounds).

Similarly, for the metacarpal region, the proximal wounds of both sides in all six horses were rinsed with physiologic saline solution and covered with gauze containing saline solution (control wounds), whereas the distal wounds were rinsed with physiologic saline solution and covered with gauze containing sunflower-seed oil (experimental wounds sunflower-seed oil Sinhá lote L 0410 GRP

201468, Brazil). In this region, all animals received the same treatment to avoid the probable interference of leakage of the oil from proximal to distal wounds.

After each treatment was applied, the wounds were kept covered by a multipurpose polycoated tape (Cremer, Blumenau, SC, Brazil) placed over gauze (Cremer) and cotton bulk (Cremer) for padding and further protection. The bandage was placed around the animal's abdomen for the lumbar lesions and around the metacarpus for wounds in the metacarpal region.

Macroscopic evaluation of the metacarpal and lumbar wounds was performed on the left-side wounds in three horses, and the right-side wounds in the other three horses. Histological evaluation was performed on the wounds located on the side opposite to those considered for the macroscopic evaluation; for example, if the right metacarpal or lumbar wounds were used for macroscopic evaluation, the left wounds were used for histological evaluation.

Subjective macroscopic evaluation (existence of edema, hyperemia, exudate, granulation tissue, and crust) and objective area measurement (image captured by a Sony Cybershot H9 digital camera (Manaus, AM, Brazil) and measured by a Starrett 727−6/150 pachymeter) were performed on the day of surgery and on days 3, 7, 14, and 21 postoperatively. The wound area was estimated according to Prata et al. [17] and Magalhães et al. [3], using the following equation:

$A = \pi \times R \times r$, where "A" represents the area, "R" represents larger measure, and "r" represents the smaller measure.

The degree of wound contraction was calculated by equations proposed by Ramsey et al. [33]:

Contraction (%) $= 100 \times (F_0 - F_A)/F_0$, where F_0 represents original area of the wound and F_A represents the area of the wound at the time of evaluation (3, 7, 14, or 21 days), expressed as a percentage.

For histopathological examination, biopsy samples were obtained using a 6-mm skin biopsy punch (Brasmed Equipamentos Veterinários, Paulínia, SP, Brazil) on days 3, 7, 14, and 21 after surgery. The skin segments included area of the wound and adjacent healthy area, and were taken around the wound to ensure none of the previous biopsy sites were included. Biopsy specimens were placed in 10% formalin and were sent for histological evaluation by a pathologist blinded to the treatment type and timing of the samples [29].

Specimens were fixed in 10% formalin for 12 hours and were then embedded in paraffin and sectioned at 4 μm (LEICA RM 2125 RT; Leica Microsystems, Nussloch, Germany). Tissue samples were stained with hematoxylin and eosin. Subjective evaluation was performed using magnification of 100× and 400× (Olympus DX51, Oympus, Tokyo, Japan), focusing mainly on features related to skin structure, such as presence of inflammatory infiltrate, exuberant granulation tissue, neovascularization, necrosis, and collagen fiber organization.

During the study period, animals were evaluated twice daily for heart and respiratory rates, body temperature, capillary refill time, color of oral and ocular mucosa, thoracic and abdominal auscultation, frequency of defecation and micturition, and appetite. During these evaluations, pain of the wounds was evaluated. The complete healing time for all wounds was recorded.

Wound area data were analyzed using analysis of variance. Comparisons between the treatments for the different periods were made using Student t test. A value of $P < .05$ was considered significant for all comparisons. All statistical analysis was performed using GRAPHPAD INSTAT 3.00 (GraphPad Software, CA, USA).

3. Results

No clinical abnormalities associated with the surgically created wounds were noted throughout the study.

The mean values for the lumbar wound area through the experimental period are listed in Table 1. A significant reduction of the wound area was evident for both groups ($P < .0001$) during the study period. Compared with the control group, the sunflower-seed oil treatment group showed a significant reduction of wound size ($P = .0216$) only on day 21. No significant differences were observed at any of the other time points ($P = .4957$ on day 3; $P = .2256$ on day 7; $P = .0519$ on day 14). Wound contraction at 21 days for the experimental group was 90.78% compared with 79.27% for the control group.

On macroscopic evaluation, wounds treated with sunflower-seed oil had a serous secretion providing a moist environment. For both treatments, granulation tissue was observed on day 7 with a thicker crust in the control group. At day 14, the control wounds showed exuberant granulation tissue with crusts on the borders. The exuberant granulation tissue was not treated in any of the wounds. The main difference between two groups was observed on day 21 when the wounds of the experimental group were almost completely healed, whereas wounds in the control group still had obvious granulation tissue (Fig. 1).

On histopathological evaluation of the lumbar wounds, the main differences between the two groups were observed on day 14 of evaluation. The control wounds had granulation tissue that was infiltrated with inflammatory cells and disorganized collagen fibers. On the evaluation done on day 21, wounds treated with sunflower-seed oil presented with a more characteristic arrangement of collagen fibers and fibroblasts, reduced inflammatory cells, and a formed capillary bed (Fig. 2).

The mean values for the metacarpal wounds through the experimental period are listed in Table 2. There was significant reduction in the wound areas for both groups (experimental group: $P < .0001$, control group: $P = .0487$).

Table 1

Mean values of wound area and contraction (C) on day 21 for lumbar wounds treated with sunflower-seed oil (experimental wounds) and control wounds, both surgically induced

Type of treatment	Day 0	Day 3	Day 7	Day 14	Day 21	C (%)
Control	19.63 ± 0.00^{a}	16.81 ± 2.81^{abA}	14.96 ± 3.46^{bA}	8.36 ± 2.89^{cA}	4.07 ± 1.70^{dA}	90.78
Experiment	19.63 ± 0.00^{a}	15.76 ± 2.31^{bA}	12.45 ± 3.27^{bcA}	5.10 ± 2.18^{dA}	1.81 ± 1.12^{dB}	79.27

Note: Different lowercase letters on the same line are significantly different ($P < .05$) on ANOVA. Different uppercase letters on the same column are significantly different ($P < .05$) on the t test.

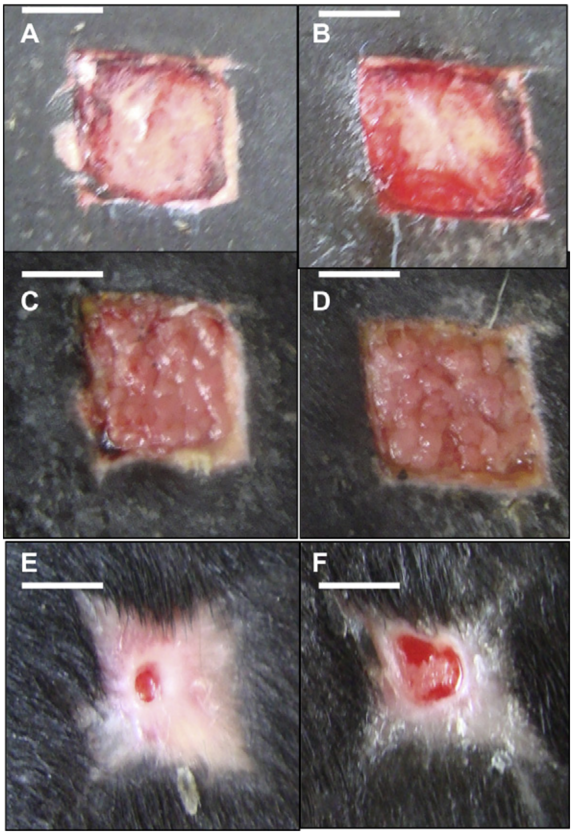

Fig. 1. Macroscopic views of lumbar wounds treated with sunflower-seed oil (**A, C, E**) and control wounds (**B, D, F**) on days 0, 7, and 21. Note granulation tissue in both groups on day 7 and almost complete healing for the treatment group on day 21. Bar: 1.25 cm.

There was no significant difference between treatments at any given period ($P = .0797$ on day 3; $P = .2346$ on day 7; $P = .0566$ on day 14; $P = .1317$ on day 21). The experimental group had a higher reduction in the wound area on day 21, but it was not statistically significant. Wound contraction in the experimental wounds was 47.63%, and in control wounds, it was 30.21%.

Similar to the lumbar wounds, the macroscopic evaluation of the treated metacarpal wounds revealed a serous secretion keeping the wounds moister. On day 14, granulation tissue was exuberant for both groups, with the experimental wounds showing the presence of crusts. The exuberant granulation tissue was not treated at any time point. On postsurgical day 21, the experimental wounds' contraction showed crusts, whereas the control group still had exuberant granulation tissue (Fig. 3).

Histopathological evaluation of the metacarpal wounds revealed differences on day 7. Both groups had granulation tissue and inflammatory cells present, but the wounds treated with the oil showed the beginning of collagen deposits. On day 14, the experimental wounds had densely organized collagen fibers, whereas the control wounds continued to have granulation tissue. By day 21, collagen fiber remodeling was evident in the experimental wounds, whereas the control wounds were still producing granulation tissue (Fig. 4).

4. Discussion

The area and depth of metacarpal and lumbar wounds were based on previously established research in horses [21,22], lambs, and rabbits [3,28,29]. Metacarpal wounds were smaller than the lumbar wounds owing to the reduced available area. All comparisons between metacarpal and lumbar wounds were made in a qualitative way.

The nonsteroidal anti-inflammatory drug (Equipalazone [phenylbutazone], Marcolab, Rio de Janeiro, RJ, Brazil) was used to reduce the pain associated with surgery in the same manner as it is used in routine clinical practice. Because it was administrated systemically, the anti-inflammatory effects would have influenced both control and experimental wounds.

The present study looked at the effects of the topical application of sunflower-seed oil on the healing process not only in wounds induced in the lumbar region but also on

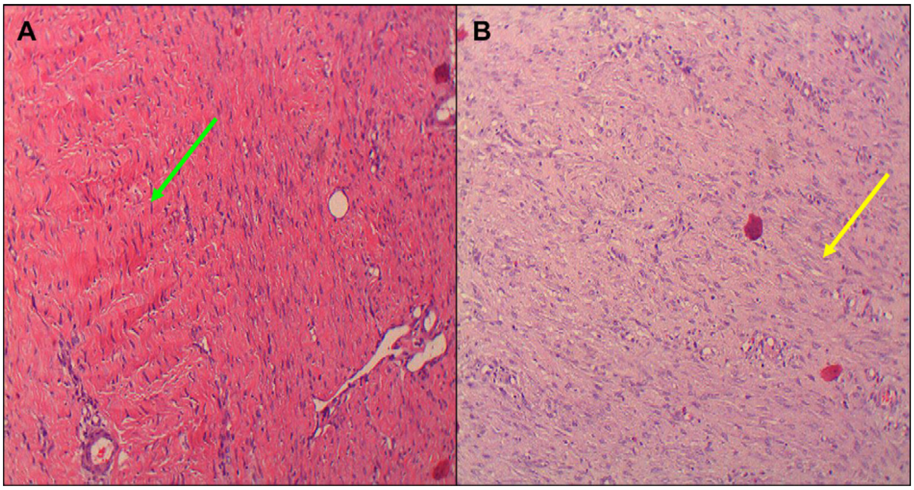

Fig. 2. Histopathological observations of lumbar wounds treated with sunflower-seed oil (**A**) and control wounds (**B**) on day 21 of the experiment. It is possible to observe presence of collagen fibers in a more regular arrangement (green arrow) in the experimental group. In the control group, it was possible that collagen fibers were still loose (yellow arrow). Photograph taken from the wound margins (100×).

Table 2
Mean values of wound area and contraction on day 21 for metacarpal wounds treated with sunflower-seed oil (experimental wounds) and control wounds, both surgically induced

Type of treatment	Day 0	Day 3	Day 7	Day 14	Day 21	C (%)
Control	9.07 ± 0.00^{a}	8.60 ± 0.29^{abA}	8.41 ± 2.22^{abA}	8.23 ± 1.76^{abA}	6.33 ± 1.96^{bA}	47.63
Experiment	9.07 ± 0.00^{a}	7.90 ± 0.83^{abA}	7.20 ± 0.75^{bA}	6.60 ± 0.58^{bA}	4.75 ± 1.31^{cA}	30.21

Note: Different lowercase letters on the same line are significantly different ($P < .05$) on ANOVA. Different uppercase letters on the same column are significantly different ($P < .05$) on the *t* test.

wounds induced in the metacarpal region, similar to the study by Souza et al. [21]. It is generally accepted that wounds on the torso will heal more effectively and functionally than a similar-sized wound on the extremities. The results of this study were found to be in agreement with previous studies when comparing wound location and healing.

Although phytotherapic products have been used to treat skin lesions in horses, little research has been done to show any beneficial effects, and there have been no published reports of using sunflower-seed oil in equine wound healing [34]. In Brazil, Souza et al. [21] described a period of 35 days for lumbar wound healing and 34 days for metacarpal wound healing when using *T vulgare*. In other research involving phytotherapics, Martins et al. [22] studied the influence of barbatimao (*Stryphnodendron barbatimao*), calendula (*Calendula officinalis*), and comfrey (*Symphytum officinale*). The authors reported a period of 21 days for barbatimao and comfrey, and a period of 26 days for calendula to induce a contraction of lumbar wounds to a final area of 0.5 mm^2. These values were comparable with those observed in the present research (21 days for lumbar wounds and 31 days for metacarpal wounds), which suggest that all these phytotherapics are beneficial to the healing process.

Marques et al. [29] and Wendt [28] evaluated the effect of sunflower-seed oil on the healing process of wounds in lambs and rabbits, respectively. Complete healing of the wounds in rabbits treated with topical application of sunflower-seed oil was observed in 18.9 days, according to Wendt [28]. His results are similar to the findings for lumbar wounds in this study, which took 21 days for complete healing. Although the use of sunflower-seed oil led to a satisfactory result, Wendt [28] did not detect differences on the healing speed, which was different from the results of Marques et al. [29] and Magalhães et al. [3]. Marques et al. [29] described an acceleration of the healing process with a reduction in the wound area and a faster

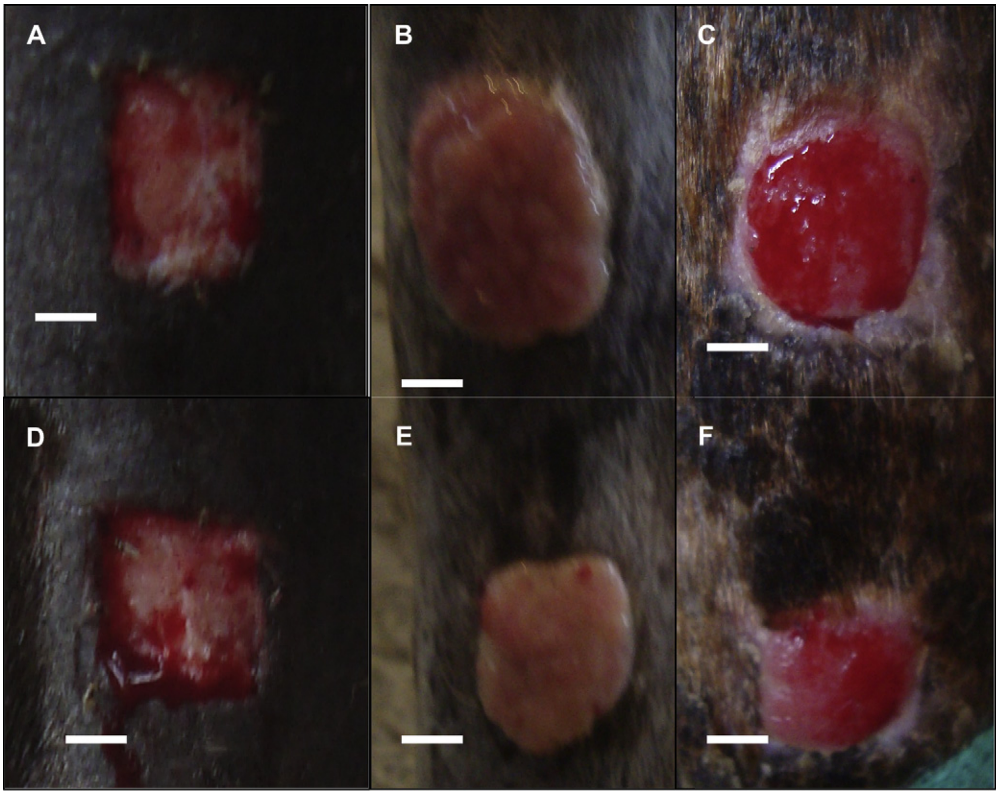

Fig. 3. Macroscopic views of metacarpal wounds treated with sunflower-seed oil (**D–F**) and control wounds (**A–C**) on days 0, 14, and 21. Note exuberant granulation tissue on day 14 mainly on the control wound. On day 21, it was possible to observe the contraction of the wound area of the wound treated with the oil. Bar: 0.7 cm.

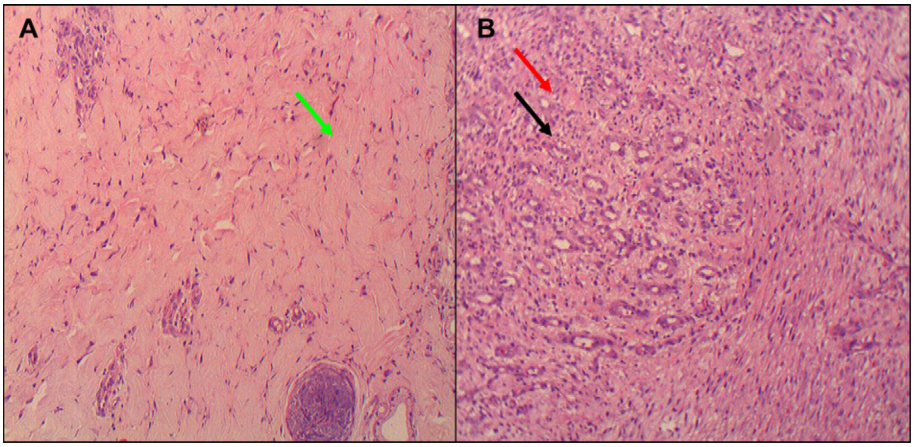

Fig. 4. Histopathologic observations of metacarpal wounds treated with sunflower-seed oil (**A**) and control wounds (**B**) on day 21 of the experiment. It is possible to observe organized collagen and dense collagen (green arrow) in the experimental group. In the control group, it was also possible to still observe the presence of inflammatory cells (black arrow) and capillary (red arrow). Photograph taken from the wound margins (100×).

contraction of the borders with a more rapid development of granulation tissue in the treated wounds compared with the control wounds. Results described by these authors are similar to those of the present research for the lumbar wounds. However, the metacarpal wounds required a longer time for complete healing (31 days) in the present study. This is possibly because of the challenges of distal limb wound healing in horses compared with that in different species. The difference in the speed of healing between lumbar and metacarpal wounds in this study was expected, as it has been shown that lumbar wounds undergo a faster healing process, with a higher centripetal contraction, thinner granulation tissue, and a faster formation of crusts compared with metacarpal wounds [21,35,36]. Stashak [37] reinforced the fact that the inflammatory process of the equine limbs is different compared with that of the torso. For example, skin lesions of 400 cm^2 in the flank have a contraction velocity of 0.8-1 mm/d, whereas similar lesions on the distal parts of the limbs contract with a velocity of 0.2 mm/d. Wilmink and Van Weeren [8] cited that wound contraction occurs by fibroblastic action (myofibroblasts) in the granulation tissue, which occurs more in body wounds.

A potential drawback in this study is the nonrandom assignment of distal limb wounds to the treatment and control groups. The sunflower-seed oil that was used had a low viscosity. The likelihood of distal contamination of the lower wounds if the oil leaked distally was deemed to be such that only the most distal wound would receive the sunflower-seed oil. Wounds areas were kept covered to ensure uninterrupted contact between the wound bed and sunflower-seed oil in the treated wounds (saline in case of the control wounds). The additional covering also protected the wounds from external agents and maintained moisture at the wound bed [38].

It is possible that the positive results obtained with the use of sunflower-seed oil in this experiment were due to the stimulation of inflammatory response, rather than because of an increase of the moisture of the wound, because controls and treated wounds were kept covered in the same way and all the wounds were moist at the bandage change. Sunflower-seed oil has in its composition linoleic acid [28], a precursor of arachidonic acid, which is important in the inflammatory cascade (prostaglandins, thromboxanes, and leukotrienes).

Granulation tissue was observed earlier in the treated wounds compared with the controls. This suggests that topical use of sunflower-seed oil possibly accelerated the cicatricial process while promoting a faster formation of granulation tissue and epithelialization, as has been described by Rocha et al. [39].

Microscopic examination confirmed an elevation in polymorphonuclear cells principally in the first few days after surgery (until day 7) on the treated wounds; this finding is similar to the results of Wilmink and Van Weeren [8] and Souza et al. [21]. The elevation of polymorphonuclear cells was also observed in the controls, but in a lower proportion. In this period of the healing process, these cells are responsible for phagocytosis of microorganisms and elimination of cellular debris, making the development of granulation tissue from the borders of the lesion easier [37]. Treated wounds had a better alignment of the collagen fibers. The main microscopic differences between control and treated lumbar lesions were observed on day 14 of evaluation for lumbar wounds and on day 21 for the metacarpal wounds.

5. Conclusion

We can conclude from the results obtained in this experiment that the topical application of sunflower-seed oil was beneficial for the healing process of experimentally induced skin wounds in horses. Wounds over the lumbar area responded best to the therapy compared with wounds in the metacarpal region. The application of sunflower-seed oil is also inexpensive [28]. The results obtained in this study suggest that sunflower-seed oil can be used as a therapeutic possibility in equine wound therapy.

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